REMARKS

Claims 13, 34 and 60 have been amended in the preamble as kindly suggested by the Examiner. Claims 14, 36 and 61 have been amended to conform to the specification; applicants apologize for the previous amendment which was inconsistent therewith. As set forth on page 21 of the specification, filtering is only applied to the query sequence (or its translation products) not to the database sequences; thus, these claims have been clarified to indicate that the second nucleotide sequence is the one that is filtered. As to the objection that coding sequences are not included, it will be noted that line 6 on page 21 refers to the sequence or its translation products, thus implicating the coding sequences. Further, the notion that commonly occurring sequences are those which are filtered out is supported on page 20, lines 15-21.

As stated above, independent claims 13 and 60 have been amended to expedite prosecution, adding two limitations which distance the claims even more strongly from the cited art. Claims 23 and 45 have been canceled as redundant. Support for the first and second nucleotide being derived from different species is found, for example, on page 5, lines 5-8, by Example 2, and throughout the specification. Support for the requirement that priority be determined by statistical analysis is found in canceled claims 23 and 45. Further, claims 13 and 60 have been amended to delete "highest identity match" since percent similarity, when 100%, will result in identical sequences. This amendment is made, also, to expedite prosecution.

No new matter has been added in these amendments and entry is respectfully requested.

Formal Matters

Applicants appreciate the clarification that the only outstanding rejections are those set forth in the Office action to which this forms a response. Applicants especially appreciate the

understanding reached at the interview that the present amendments are sufficient clearly to distinguish the pending claims from the cited art.

All claims were rejected (it is assumed claim 34 was inadvertently omitted from the list) as containing new matter based on the requirement in claims 13, 34 and 60 that the prioritizing of the extracted gene sequence is based on identity match *and* percent similarity. The Office asserts that there is no basis for this in the specification because beginning on page 29, the specification "lists numerous sequence comparison tools" wherein "not all alignment programs prioritize sequences in an alignment based on identity *and* percent similarity." (Emphasis in the original.)

The claims have been amended to focus on percent similarity; including percent identity is not excluded since the claims refer to "at least a percent similarity." However, the specific grouping of these two criteria is no longer included in the claim.

In any event, it is not seen why inclusion of both identity and percent similarity would constitute new matter. It is perfectly possible to apply more than one alignment tool in prioritizing the extracted sequences. Thus, it is not a requirement that each alignment tool set forth in the specification employ both comparison systems. Further, it is noted that on page 60, line 20, a retrieved sequence is compared to a known sequence on the basis both of identity and similarity. These are common comparison tools, as is recognized by the Office, and the rationale offered by the Office does not lead to the conclusion that this is new matter. In any event, amendment has been made so that it is clear that this basis for rejection may properly be withdrawn.

With regard to claims 14, 36 and 61, the support for "which are regions commonly found in encoding nucleotide sequences" has been pointed out above as set forth on page 20, lines 15-21. This phrase does not appear *in haec verba*, but it is clear from the context that this

phrase is supported by the description in the specification. Accordingly, this basis for rejection, too, may be withdrawn.

Finally, with respect to claims 13, 34 and 60 as rejected under 35 U.S.C. § 112, second paragraph, applicants appreciate the suggestion provided by the Examiner and have amended the claims in accordance with it.

The Rejection Over the Art

All claims were rejected as assertedly obvious over the combination of U.S. patent 6,303,297 with Rose, *et al.* In view of the discussion at the interview and the amendment to the claims, the following discussion may be moot; however, applicants wish to make of record that the claims, even before amendment, were not suggested by the cited art.

First, it should be pointed out that the claims are directed to a specific sequence of steps which are required to be followed in order to practice the invention. Specifically, the invention comprises the steps of:

1. Identifying a particular nucleotide sequence that is associated with a desired phenotypic characteristic.

2. Using the nucleotide sequence of step 1 as a query to identify sequences in a cataloged database that a) match at least a portion of the query and b) are annotated to have the desired phenotypic characteristic.

3. Extracting any cataloged nucleotide sequences thus identified.

4. Prioritizing the extracted nucleotide sequences based on any number of alignment tools where those with at least highest similarity have the highest priority.

5. Using the high priority extracted sequences to design primers for cloning.

A dependent claim in each case requires filtering the query sequence to eliminate non-informative portions.

The Office has correctly stated certain features of the primary document. But there appears to be nothing in the primary document that describes the steps in the independent claims. The design of primers is not the only step missing. Applicants cannot agree that Lincoln discloses steps 1 through 4 and that all that remains is to combine Lincoln with any document that describes the design of primers in order to suggest the claimed subject matter. First, it should be clear that there is no step 2, which requires that the query sequence be matched with a portion of a cataloged sequence and that the cataloged sequence exist in the database as annotated for a desired phenotypic characteristic before it is retrieved. As should be evident by Example 1 in the Lincoln patent, it is the query sequence that is used to annotate the database with regard to phenotypic characteristics; the database is not already annotated for phenotypic characteristics when the query is made, unlike the present invention. There is no step 4 of prioritizing the retrieved sequence with respect to the query sequence to arrange a collection of retrieved sequences so as to obtain high priority sequences. The query merely results in the annotation of the database, which already contains "clusters" of sequences. Certainly there is nothing in the '297 patent that describes the claimed sequence of steps. Indeed, the '297 patent appears simply to be directed to, as its title states, a "Database for Storage and Analysis of Full-Length Sequences."

The only even relevant portion of the '297 document (over and above the bioinformatics tools already discussed in the present specification) is the example of gene discovery – at least a more-or-less common problem with that of the invention is being tackled . However, it will be noted that the example cited by the Office is quite different from the steps set forth in the claims. Although a phenotypic characteristic was associated with a query sequence, this was then used to find similar clustered sequences in a database which, by virtue of their similarity to the query, were then postulated to serve the same function. The queried database sequences are not

annotated for phenotype as required by the claims. Instead, the query sequence is used to annotate the database. The retrieved sequences are not prioritized; they have already been "clustered." And there is no suggestion in Lincoln that the sequences in the database be used to retrieve an entirely new sequence not in the database, by any method whatsoever.

The Rose article cited by the Office relates to the design of primers by combining two compromise techniques. The primers contain a degenerate region which is reasonably certain to match a targeted nucleotide sequence at the 3′ portion to be extended, but a non-degenerate consensus sequence which may not match as well at the 5′ end. These primers are not suggested to be designed by the method of the invention, but rather by simply assembling data from cataloged databases and using a collection of sequences to design the two aspects of the resulting primers. There is no real description in Rose of how one arrives at the regions to be represented in the degenerate and consensus portions of the primer. The disclosure of Rose simply gives details of how one might design primers based on matching portions of any aligned sequences.

Thus, the combination of Rose with the '297 patent, even if made, does not result in the invention, because the '297 patent does not suggest the sequence of steps up to step 5, the only step with which Rose is even concerned.

Further, there appears to be no motivation to combine these two documents specifically. The motivation asserted by the Office is that the '297 patent states that the database can be useful for a variety of things, including identification of genes. It is not seen how this statement suggests combination with a document which is concerned with the design of primers. Lincoln has already reached the end point of gene identification when sequences already in the database are recognized as similar to a query sequence of known function. There is no suggestion at all in Lincoln to use the database contained sequences for anything else. Rose could be putatively combined with any relational database; the claims are not directed to combining relational

databases with primers, but rather to a specific set of steps in deriving a means for designing primers from known relational databases.

It is noted that certain dependent claims, for example, claims 17, 19, 23, 25 and 26, and the corresponding claims dependent from claims 34 and 60 are not specifically addressed in the rejection.

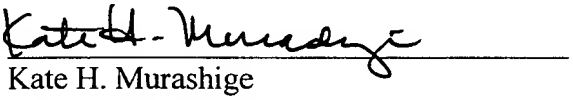
For the reasons set forth above, applicants respectfully submit that this basis for rejection may properly be withdrawn.

CONCLUSION

The documents upon which the sole art rejection is based, even when combined, fail to suggest the specific set of steps required in the claimed invention method and system. Further, no credible motivation to combine these documents has been asserted. Nevertheless, the claims have been amended as agreed at the interview to expedite prosecution. Applicants again wish to express their appreciation to Examiners Clow and Fredman for their help in this regard. The discussion at the interview was most appreciated. Thus, applicants respectfully submit that all pending claims are free of the art and in a position for allowance. Applicants respectfully request these claims be passed to issue forthwith.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 524412000200.

Respectfully submitted,

Dated: November 26, 2003 By: 

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